

**REMARKS**

Claims 31 and 34-54 are currently pending in the captioned application. Applicants wish to thank Examiner Steele for the courtesy of the telephonic interview on June 7, 2010 to discuss the currently rejected claims. During the telephonic interview, the Examiner indicated that that the terms "subtractor/target ligand construct" were not clear. Applicants have amended the claims to include the definition of "subtractor/target ligand construct," which can be found in [0089] of the specification. As suggested by the Examiner, the claims have also been amended to indicate that step (iv) of claim 31 is performed to determine the amounts of subtractor ligand to be added as compared to target ligand to identify an anti-ligand to at least one target ligand. The claims have also been amended to replace "using" in step (ix) with "utilizing."

The claims have been amended to more particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully submit that the amended claims are supported by the original disclosure of this application. As such, no new matter has been added by these amendments. Reconsideration of this application is respectfully requested.

**1. Claim Rejections Under 35 USC § 112, Second Paragraph**

Claims 31 and 34-54 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, Applicants failed to point out support for previous amendments made to the claims. Specifically, step (ii) of claim 31 was amended to read "providing a first population of ligands comprising a ligand fixed to or incorporated in a subtractor ligand construct" and step (iii) to read "providing a second population of ligands comprising the same ligand as step (ii), fixed to or incorporated in a target

ligand construct. Support for this amendment can be found in [0029]-[0039] and [0089] of the specification.

Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

**2. The Claims Are Not Anticipated**

The rejection of Claims 31, 34-35, and 38-54 under 35 U.S.C. 102(e) as being anticipated by Lonberg et al. U.S. Patent 7,135,287 ("Lonberg") is maintained by the Examiner.

According to the Examiner, for present claims 31, 34-35, and 38-39, Lonberg teaches display selection methods to screen libraries of human immunoglobulins comprising: (i) providing a library of antibodies, ii-iii) providing ligands including ligands for negative selection, prescreening, and/or targets including antigens, (iv-vi) utilizing the universal law of mass action to determine the amount of ligands, (vii) separating antibodies from ligands, and (viii-ix) repeating the selection and separation steps. Regarding the equations in claims 31 and 38-39, since applicants elected a wet bench method, these steps equate to a mental process (i.e. mathematical manipulation). See MPEP § 2111 and *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969). Therefore, according to the Examiner, the teachings of Lonberg et al. anticipate the presently claimed method.

Applicants assert that the currently pending claims, as amended, are not anticipated by Lonberg. The key difference between Lonberg and the currently claimed invention is the application of the law of mass action and the listed equation as part of the method that represents the invention. As the amended claims specify, the law of mass action is utilized to determine the amounts of subtractor ligand versus the amount of target ligand to be used to result in efficient identification of anti-ligands that bind to a target antigen of interest. As stated in [0105] of the specification, "applying the Universal Law of Mass Action (LMA), the number of ligands

needed to isolate anti-ligands to low expression ligands and/or differentially expressed ligands from display libraries of high diversity may be calculated.” Thus, the invention provides an efficient method for identifying a target ligand that is differentially expressed, including ligands that are expressed and upregulated at low levels in one ligand population as compared to another. Such ligands may include, for example, cell surface proteins differentially expressed on the surface of cells, e.g. cancer versus normal cells. The claimed method as a whole is not directed to merely a mental process but rather to a method for isolating at least one anti-ligand to at least one target ligand, wherein said method utilizes the equation recited in the claim.

In contrast to the present invention, Lonberg fails to disclose or even suggest the use of the LMA to identify low expression ligands or differentially expressed ligands from display libraries. Rather, Lonberg’s disclosure of the use of LMA, in column 26, lines 27-37 of the specification, is designed to select “between antibody chains of different monovalent affinities for the target...” (see, col. 26, lines 20-23 of Lonberg). Given the differences between the presently pending claims and the disclosure of Lonberg, the claims cannot be anticipated by Lonberg. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

### **3. The Claims Are Not Obvious**

Claims 31 and 34-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lonberg and U.S. Patent 6,794,128 (“Marks”).

According to the Examiner, although Lonberg does not specifically teach utilizing an excess of one ligand over another ligand. Marks teaches methods of selecting phage displayed antibodies comprising contacting target cells with a phage display antibody library and also

contacting the phage display antibody library with subtractive cells wherein the subtractive cells are in at least a 2 fold excess of the target cells and including 100 fold or 1000 fold excess.

According to the Examiner, the claims would have been obvious because a particular known technique (i.e. subtractive screening of an antibody phage displayed library with 100 fold excess of subtractor to target as taught by Marks et al.) was recognized as part of the ordinary capabilities of one skilled in the art.

As set forth above, the currently pending claims are directed to a method for isolating at least one anti-ligand to at least one target ligand, wherein said method utilizes the equation recited in the claim to determine the amounts of subtractor ligand versus target ligand to be used. Lonberg fails to disclose or suggest such a method, therefore, the claims cannot be rendered obvious by Lonberg. The disclosure or suggestion of the present claimed invention that is absent from Lonberg is not supplied by Marks. Although Marks may disclose the use of excess subtractor cells over target cells for screening purposes, Marks fails to disclose a method for determining the amounts of subtractor cells versus target cells to be used efficiently to identify differentially expressed ligands. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

**Conclusion**

In view of the remarks made hereinabove, Applicants respectfully request that the Examiner reconsider and withdraw the rejections set forth in the November 18, 2008 Office Action, and earnestly solicits allowance of the now pending claims.

If a telephone interview would assist in expediting prosecution of the subject application, the Examiner is invited to telephone the undersigned at the number provided below. No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 11-0600.

Respectfully submitted,  
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